REMARKS

Under an *Ex parte Quayle* action, the Examiner kindly indicates that Claims 1-7 and 12-21 are allowed and the application is in condition for allowance except for formal matters regarding cancellation of the nonelected invention. In response, Applicants are currently canceling nonelected Claims 8-11. It is reiterated that Applicants reserve the right to file a divisional application directed to the nonelected subject matter of the present invention.

Applicants look forward to receipt of the Notice of Allowance with gratitude and wish to thank the Examiner for the favorable treatment of this application.

Respectfully submitted,

WYETH

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APPENDIX

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

Claim 1 (Previously presented). A method for synthesis of 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-disulfonic acid, the process comprising the steps of:

a) reacting 2-(3-Nitro-benzenesulfonylamino)-acetamide with $ClCH_2CONH_2$ in the presence of N,N-Dimethylformamide and a base to provide 2-[Carbamoylmethyl-(3-nitro-benzenesulfonyl)-amino]acetamide;

b) treating the 2-[Carbamoylmethyl-(3-nitro-benzenesulfonyl)-amino]acetamide product of step a) with a reducing agent to provide 2-[(3-Amino-benzenesulfonyl)-carbamoylmethyl-amino]acetamide;

c) treating the 2-[(3-Amino-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product of step b) with cyanuric chloride to give 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide; and

d) reacting the 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product of step c) with the disodium salt of 4,4'-diamino-2,2'-biphenyldisulfonic acid.

Claim 2 (Original). The method of Claim 1 wherein the treatment of 2-[(3-Amino-benzene-sulfonyl)-carbamoylmethyl-amino]acetamide with cyanuric chloride to give 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide is conducted at a temperature of from about 20°C to about 25°C.

Claim 3 (Original). The method of Claim 1 wherein the treatment of 2-[(3-Amino-benzene-sulfonyl)-carbamoylmethyl-amino]acetamide with cyanuric chloride to give 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}benzenesulfonyl)-carbamoylmethyl-amino]acetamide is conducted in a reaction medium containing 1-methyl-2-pyrrolidinone and sodium carbonate or sodium bicarbonate.

Claim 4 (Original). The method of Claim 1 further comprising the step of recrystallizing the 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product of step c) from a mixture of 1-methyl-2-pyrrolidinone and water prior to completing the reaction of step d).

Claim 5 (Original). The method of Claim 1 wherein step d) is conducted at a temperature of from about 15°C to about 90°C.

Claim 6 (Original). The method of Claim 5 wherein step d) is conducted at a temperature of from about 60°C to about 75°C.

Claim 7 (Original). The method of Claim 1 wherein step d) is conducted in a medium comprising dimethyl sulfoxide.

Claim 8 (Canceled).
Claim 9 (Canceled).
Claim 10 (Canceled).
Claim 11 (Canceled).

Claim 12 (Original). A process for purifying 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide obtained by treating 2-[(3-amino-benzenesulfonyl)-carbamoylmethyl-amino]-acetamide with cyanuric chloride, which comprises dissolving 2-[(4-{4-[4-(bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-

carbamoylmethyl-amino]acetamide in a volume of water and 1-methyl-2-pyrrolidinone, followed by addition of excess water to precipitate a more purified amount of 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide.

Claim 13 (Previously presented). The process according to Claim 12 wherein the ratio of water:1-methyl-2-pyrrolidinone into which the amount of 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]-acetamide is dissolved is from about 1:1 by weight.

Claim 14 (Previously presented). The process according to Claim 12 wherein precipitation of the desired 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product is carried out by adding additional water to create a water:1-methyl-2-pyrrolidinone ratio of up to about 6:1 (wt:wt).

Claim 15 (Previously presented). The process according to Claim 13 wherein precipitation of the desired 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product is carried out by adding additional water to create a water:1-methyl-2-pyrrolidinone ratio of up to about 6:1 (wt:wt).

Claim 16 (Previously presented). The process according to Claim 14 wherein precipitation of the desired 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product is carried out by adding additional water to create a water:1-methyl-2-pyrrolidinone ratio from about 3:1 to about 5:1 (wt:wt).

Claim 17 (Previously presented). A process for the increasing the purity of 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-disulfonic acid, disodium salt which comprises dissolving impure 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-

disulfonic acid, disodium salt in volume of acetonitrile-water having a mixture ratio of from about 0.75:2 to about 1.5:2 by volume at an elevated temperature of from about 30°C to about 70°C, followed by addition of additional acetonitrile until crystallization of the desired compound is achieved.

Claim 18 (Previously presented). The process according to Claim 17 wherein the elevated temperature is from about 60°C - about 70°C and after the addition of additional acetonitrile the mixture is cooled to about 49°C - about 51°C.

Claim 19 (Previously presented). The process according to Claim 1 in which the 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-disulfonic acid, disodium salt prepared is purified by dissolving impure 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-disulfonic acid, disodium salt in volume of acetonitrile-water having a mixture ratio of from about 0.75:2 to about 1.5:2 by volume at an elevated temperature of from about 30°C to about 70°C, followed by addition of additional acetonitrile until crystallization of the desired compound is achieved.

Claim 20 (Previously presented). The process according to Claim 19 in which the 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-disulfonic acid, disodium salt prepared is purified by dissolving impure 4',4-bis-{4,6-bis-[3-(bis-carbamoyl-methyl-1-sulfamoyl)-phenylamino]-[1,3,5]triazin-2-ylamino}-biphenyl-2,2'-disulfonic acid, disodium salt in volume of acetonitrile-water having a mixture ratio of from about 0.75:2 to about 1.5:2 by volume at an elevated temperature of from about 60°C to about 70°C, followed by addition of additional acetonitrile and cooling of the mixture to a temperature of from about 49°C to about 51°C until crystallization of the desired compound is achieved.

Claim 21 (Previously presented). The process according to Claim 16 wherein precipitation of the desired 2-[(4-{4-[4-(Bis-carbamoylmethyl-sulfamoyl)-benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl}-benzenesulfonyl)-carbamoylmethyl-amino]acetamide product is carried out by adding additional water to create a water:1-methyl-2-pyrrolidinone ratio of about 4:1 (wt:wt).